AF

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/998,250	11/30/2001	Shoukat Dedhar	KINE001CIP5	5685

24353 7590 02/06/2006

BOZICEVIC, FIELD & FRANCIS LLP
1900 UNIVERSITY AVENUE
SUITE 200
EAST PALO ALTO, CA 94303

EXAMINER	
WILLIAMS, LEONARD M	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 02/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/998,250	DEDHAR ET AL.	
	Examiner	Art Unit	
	Leonard M. Williams	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1 and 15-22 is/are pending in the application.

4a) Of the above claim(s) 15-22 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Status of the Claims

The examiner notes receipt on 11/04/2005 of the applicant's remarks and amendments to the claims. Canceling claim 13 and amending claim 1. New claims 15-22 have been added.

Claim 1 is pending.

Claim 13 is currently cancelled.

Claims 2-12 were previously cancelled.

New claims 15-22 have been added, but are not addressed due to original presentation.

Response to Amendment

The amendment of claim 1 removing the term "...specifically inhibits..." is sufficient to overcome the 112-2 rejection of claim 1. The 112-2 rejection of claim 1 is withdrawn.

The amendment of claim 1 to remove the term "...chronic inflammation..." and insert the term "...psoriasis..." is sufficient to overcome the 112-1 scope of enablement of chronic inflammation rejection of claim 1. The 112-1 scope of enablement of chronic inflammation is withdrawn.

Response to Arguments

Applicant's arguments filed 11/04/2005 have been fully considered and are specifically addressed below.

The applicant's traverse the 112-1 scope of enablement on the small organic molecules on the basis that the level of experimentation to identify specific inhibitors is routine, and readily performed by one of ordinary skill in the art. The applicant's further assert that the small organic molecules described by Anderson and Zhang demonstrate that one of skill in the art can readily identify a number of useful molecules for inhibition of ILK. The examiner agrees with the applicant that ILK inhibitors can be found and that Anderson and Zhang provide some small organic molecules that can inhibit ILK either directly or indirectly. The examiner respectfully points out that the present application only provides enablement for the specific compounds of US Patent 6214813, MC-5, wortmannin and LY294002 in a method of treating psoriasis and only exemplifies one of these compounds in the application in an inflammation assay. The applicant's have not provided sufficient description and evidence to allow for all ILK inhibitors. The 112-1 scope of enablement of small organic molecules of claim 1 is thus maintained. The 112-1 scope of enablement of small organic molecules of claim 1 is reproduced below.

The 102(b) and 102(e) rejections of claim 1 have been withdrawn as necessitated by the amendment of claim 1. A new rejection of claim 1 is detailed below.

Election/Restrictions

Newly submitted claims 15-22 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: New claims 15-19

are drawn to a method of treating psoriasis comprising administration of an ILK inhibitor and a second therapy for psoriasis. There are a plurality of compounds (and therapies) listed as the second therapy for psoriasis. New claims 20-22 is drawn to a method for treating psoriasis comprising staining to determine the expression of ILK then administering an inhibitor of ILK. If these claims were originally presented they would have been restricted as distinct inventions.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 15-22 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Priority

Examiner notes that the current application is a continuation-in-part (CIP) of 09/390425 now US Patent 6338958 which is a continuation of 09/035706 now US Patent 6001622 which is a CIP of 08/955841 now US Patent 6013782 which is a CIP of 08/752345 now abandoned which claims benefit to provisional application 60/009074.

The examiner notes that US Patent 6338958 (from application 09/390425) of which the current application is a CIP mentions "small organic molecules" that can inhibit ILK activity in col. 10 lines 5-45. In col. 10 lines 17-26 two specific small molecules are mentioned, wortmannin and LY294002, both of which are clearly stated as agents of interest even though they are inhibitors of PI(3) kinase and not ILK.. No additional small organic molecules are mentioned in US Patent 6338958.

The present application is directed to methods of treating inflammation by administration of ILK inhibitor compounds. On pages 4 and 5 of the current application "small organic compounds" that block ILK catalytic or binding activity either directly or indirectly are said to be described in US Patent 6214813 (which has no common inventors or assignee with the current application) which is incorporated by reference thus admitting it as prior art. Additionally applicant incorporates by reference US Patent 6177273 drawn to antisense inhibitors of ILK and restates that wortmannin and LY294002 are agents of interest. In examples 3 and 4 of the current application the applicant details the use of a small molecule anti-ILK compound called MC-5 in the treatment of an acute mouse ear-swelling edema model of inflammation. Compound MC-5 is not described nor previously mentioned in the present or previous applications. As there is a lack of description of the ILK inhibitor compounds of US Patent 6214813 (incorporated by reference in the current application) and the MC-5 compound in the parent application these compounds receive only the current applications filing date of 11/30/2001 for prior art purposes. Wortmannin and LY294002 are given the filing date of the earlier application 03/05/1998.

The examiner further points out that the use of ILK inhibitors in methods of treating psoriasis is first mentioned in the present application. Thus methods of treating psoriasis with ILK inhibitors is only given the current applications filing date.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Scope of Small Organic Molecule

Claims 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the ILK inhibitor compounds of US Patent 6214813, wortmannin, LY294002, and MC-5 does not reasonably provide enablement for "...wherein said ILK inhibitor is a small organic molecule...". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the ad; (4) the predictability or unpredictability of the ad; (5) the breadth of the claims', (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The Nature of the Invention:

The rejected claims are drawn to "A method for treating chronic inflammation, the method comprising: topically administering an effective amount of an inhibitor of integrin linked kinase (ILK) wherein said ILK inhibitor is a small organic molecule that specifically inhibits ILK activity".

(2) Breadth of the Claims:

The breadth of the claims are exceptionally broad encompassing any "...small organic molecule..." examples could include methane, ethane, ethanol, aspirin, etc...there are no clear structural/functional limitations.

(3) Guidance of the Specification:

The guidance of the specification as to "a small organic molecule" is limited to the ILK inhibitor compounds of US Patent 6214813, wortmannin, LY294002, and MC-5. Though the examiner notes that there is no description as to what MC-5 is, i.e. no chemical name or structure or reference where such information exists.

Compounds possessing other activities are not described in an enabling fashion.

(4) Working Examples:

The applicant provides working examples in example 3 and 4 of the specification for the compound MC-5. The ILK inhibitor compounds of US Patent 6214813 provide

examples enabling the particular compounds therein, wortmannin and LY294002 are well know GSK1 inhibitors.

(5) State/predictability of the Art:

The state of the art regarding "a small organic molecule" and its subsequent testing as an inhibitor of ILK or any receptor is high. As the breadth of the term "a small organic molecule" is enormous encompassing a myriad of different structures.

(6) The Quantity of Experimentation Necessary:

The instant claims read on any small molecule. As discussed above, the specification fails to provide sufficient support for agents other than the ILK inhibitor compounds of US Patent 6214813, wortmannin, LY294002, and MC-5. Applicant fails to provide information sufficient to practice the claimed invention, absent undue experimentation (i.e. experimenting with all small organic compounds). Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Accordingly the claims are evaluated as being drawn to the a method for treating chronic inflammation comprising "a small organic molecule" limited to the ILK inhibitor compounds of US Patent 6214813, wortmannin, LY294002, and MC-5

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bonjouklian et al. (US Patent 5378725), in view of Zhang et al. (Up-regulation of phophatidylinositol 3-kinase in psoriatic lesion, 1999, Chinese Medical Journal, vol. 112, iss. 12, pp. 1097-1100) and further in view of applicant's own admission.

Bonjouklian et al. teach, in col. 6 lines 10-60, that wortmannin is an inhibitor of phosphatidylinositol 3-kinase (a kinase involved in mitogenesis, cellular proliferation, and cellular differentiation) useful in the treatment of a variety of PI 3-kinase dependent biological processes including pain, diabetes, inflammation, platelet aggregation, vascular diseases, atherosclerosis (a chronic inflammatory disorder), and restenosis. Bonjouklian et al. teach in col. 7 lines 5-20, that wortmannin can be formulated into pharmaceutical compositions for parenteral, transdermal, rectal, nasal, intravenous or oral administration.

Bonjouklian et al. does not specifically teach the use of wortmannin in the treatment of psoriasis. Nor does Bonjouklian et al. teach wortmannin as an inhibitor of ILK.

Zhang et al. teach on page 1097 that PI 3-kinase is up regulated in psoriatic lesions (as compared to normal skin) and that the over-expression of PI 3-kinase may be related to the hyperproliferation of psoriatic keratinocytes.

The applicant's state on page 5 of the specification:

"Because ILK activity is up regulated by the presence of the lipid [PtdIns(3,4,5)P.sub.3], the activity of ILK can be manipulated by agents that affect cellular levels of [Ptdins(3,4,5)P.sub.3], or that block the binding of [PtdIns(3,4,5)P.sub.3] to ILK. The amino acid sequence of ILK contains a sequence motif found in pleckstrin homology (PH) domains, which are involved in the binding of phosphatidylinositol phosphates. The activity of ILK is also down regulated by inhibiting the activity of PI(3) kinase, thereby decreasing cellular levels of [Ptdins(3,4,5)P.sub.3]. Agents of interest include inhibitors of PI(3) kinase, e.g. wortmannin, LY294002, etc. Physiologically effective levels of wortmannin range from about 10 to 1000 nM, usually from about 100 to 500 nM, and optimally at about 200 nM. Physiologically effective levels of LY294002 range from about 1 to 500 .mu.M, usually from about 25 to 100 .mu.M, and optimally at about 50 .mu.M. The inhibitors are administered in vivo or in vitro at a dose sufficient to provide for these concentrations in the target tissue."

It would have been obvious to of ordinary skill in the art at the time the invention was made to use wortmannin as a small organic molecule inhibitor of ILK in a method of treating psoriasis, as wortmannin was shown to be an inhibitor of PI 3-kinase (Bonjouklian et al.), PI 3-kinase was up-regulated in psoriatic lesions (Zhang et al.), and PI 3-kinase inhibitors were known to down regulate the activity of ILK.

The motivation to use wortmannin as an inhibitor of ILK activity in the treatment of psoriasis is that wortmannin has been formulated as a pharmaceutical agent for both oral and dermal administration (Bonjouklian et al.), PI 3-kinase is known to be up-

regulated in psoriatic lesions, wortmannin is an inhibitor of PI 3-kinase and inhibition of PI 3-kinase down regulates ILK. Thus one would be motivated to apply pharmaceutical compositions comprising wortmannin to treat psoriasis either as a direct inhibitor of PI 3-kinase or an indirect inhibitor of ILK.

The examiner respectfully points out the following from MPEP § 2112.01: "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leonard M. Williams whose telephone number is 571-272-0685. The examiner can normally be reached on MF 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

LMW

SHENGJUN WANG
SUPERVISORY EXAMINER